DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 3/28/11 and 10/4/11 has been entered.

Claims 1 and 27 have been amended.

Claims 41-55 have been added.

Claims 1-31 and 35-55 are pending.

2. Applicant's election with traverse of a suspension as the species of composition, and polyethylene glycol as the species of carrier/binder/diluent, in the reply filed on 1 is acknowledged.

Applicant's traversal is on the grounds that it would not be an undue burden to examine all the species together. This is not found to be persuasive because the claims are drawn to structurally different compositions such as a solid table, or a solution, and compositions distinct carriers such as media, polymers, lipids etc. Therefore these compositions are distinct, and searches for all would place an undue burden upon the examiner. It is an undue burden for the examiner to search more than one invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-26, 30, 39, and 54-55 are withdrawn from further consideration pursuant to 37 CFR 1.14209 as being drawn to a nonelected invention. Applicant indicates that claims 27-29, 31, 35-38, 40-46, and 48-53 read on the elected species. However, claim 44 is drawn to a composition wherein the

carriers are various other mediums, and the elected carrier is polyethylene glycol. Furthermore, Claim 48 depends from claim 47, which Applicant indicates does not read on the elected species. Additionally, claim 50 is drawn to a composition comprising different carriers than the elected carrier of polyethylene glycol, while claim 52 is drawn to a finely divided solid carrier, which is distinct from a solution comprising polyethylene glycol. Regarding claim 43, it is noted that the claim is being included in the examination to the extent that the claim recites a composition in the form of a "bolus" which is deemed to read on a solution comprising polyethylene glycol. Likewise, claim 46 is being included to the extent that it recites a dosage enclosed in ampoules, syringes, or vials. Claim 51 is being included to the extent that it recites a "dispersion media". Claims 44, 47-48, 50, and 52 are withdrawn from further consideration as being drawn to nonelected species. Upon reconsideration, the examination is being extended to include compositions comprising a nucleic acid encoding IL-12.

Claims 27-29, 31, 35-38, 40-43, 45-46, 49, 51, and 53 are under examination as they read on the elected species.

3. In view of Applicant's amendment and remarks, the rejection of the claims under 35 U.S.C. 102 as being anticipated by Kelleher et al. is withdrawn.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 27-29, 31, 35-38, and 40 stand rejected, and claims 41-43, 51, and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhardwaj et al., 1996, as evidenced by Hackstein et al., 2002.

As set forth previously, Bhardwaj et al. disclose a culture (i.e. a composition) comprising ex-vivo purified dendritic cells and IL-12 (see pg. 715 and Table 1 in particular). As evidenced by Hackstein et

al., dendritic cells arise from CD34+ stem cells, and thus the ex-vivo isolated dendritic cells taught by Bhardwaj et al. are CD34+ derived. It is noted that the term “therapeutic composition” carries little patentable weight in the absence of evidence of a structural difference, since it refers to an intended use of the composition. The culture medium taught by Bhardwaj et al. (RPMI supplemented with gentamicin, human serum and HEPES buffer) is not incompatible with biological activity and therefore meets the limitations of a “therapeutic composition”.

Applicant’s arguments filled 3/28/11 have been fully considered, but they are not persuasive.

Applicant argues that the composition of Bhardwaj et al. comprises human serum, which does not meet the limitation of a composition with a "standard of purity and quality control required for administration to humans".

Applicant has not provided any evidence that human serum is contraindicated for administration to humans, via a topical route for example. In fact, as evidenced by U.S. patent 6,498,006 and U.S. patent 5,140,104, human serum and serum components can be used as a pharmaceutically acceptable carrier for administration to human subjects (see column 9, lines 10-19, of the ‘006 patent and column 15, lines 57-65 of the ‘104 patent, in particular). Bhardwaj et al. teach a composition comprising dendritic cells, IL-12, and tissue culture medium (i.e. a solution) that meets the limitations of the instant claims, as set forth in the decision by the BPAI on 1/28/11.

It is noted that claims 41-43 and 51 are bind included in the rejection since the tissue culture medium of Bhardwaj et al. can be considered an "inert diluent" or "dispersion media". Furthermore, cells in culture medium can be considered a suspension, or are in the form suitable for a “bolus” administration. Additionally, claim 53 is being included, since the instant claims are drawn to a product, a composition comprising dendritic cells, and the manner in which the dendritic cells are obtained (i.e. by culture ex-vivo with cytokines) does not carry patentable weight in the absence of a structural difference in the product. In the instant case, the CD34+ derived dendritic cells of Bhardwaj et al. are structurally identical to those of the instant claims, though produced by a different process (i.e. direct isolation of in vivo differentiated dendritic cells).

6. The following are new grounds of rejection.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 27-29, 31, 35-38, 40-43, 51, and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/15264 (of record).

WO 00/15264 teaches a composition that can be administered for therapy, wherein said composition comprises a dendritic cell that has been genetically modified to comprise a nucleic acid encoding an immunostimulatory cytokine (see page 3 and 6, in particular). WO 00/15264 teaches administering said compositions therapeutically wherein the dendritic cells are not pre-loaded or pulsed with antigen (see page 6, in particular). WO 00/15264 teaches IL-12 as the immunostimulatory cytokine. WO 00/15264 teaches administering the dendritic cells in a physiologically acceptable solution or buffer and for the treatment of human subjects (i.e. in the form of a suspension that complies with standards required for administration to humans, see page 8). Said physiologically acceptable buffer can be considered an “inert diluent”, or “dispersion media”. WO 00/15264 teaches administration by injection. A solution comprising a buffer and a dendritic cells for injection can be considered a "bolus". WO 00/15264 teaches producing the CD34 derived dendritic cells by culture with Flt-3 ligand or GM-CSF and IL-4 (see paragraph 9, in particular).

Thus, the reference clearly anticipates the invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be

> patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27-29, 31, 35-38, 40-43, 45-46, 51, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/15264 (of record), in view of U.S. Publication 20020091246.

The teachings of WO 00/15264 are described above.

WO 00/15264 does not teach a carrier comprising polyethylene glycol.

The ‘246 publication teaches therapeutic compositions comprising dendritic cells can be administered in a variety of pharmaceutically acceptable diluents, including polyethylene glycol (see page 19, in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to prepare the therapeutic compositions of WO 00/15264, using a pharmaceutically acceptable diluent comprising polyethylene glycol, as taught by the '246 publication. Selecting from the known diluents would involve choosing among a finite number of predictable options which could be pursued with a reasonable expectation of success. A person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense (see *KSR International Co. V. Telefex Inc* 82 USPQ2d 1385). Furthermore, it would have

been obvious to enclose the dendritic cell suspension of WO 00/15264 in a disposable syringe for injection.

9. Claims 27-29, 31, 35-38, 40-43, 46, 49, 51, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/15264, in view of Brunda et al., 1993 (of record) and U.S. Patent 5,583,714.

The teachings of WO 00/15264 are described above. WO 00/15264 also teaches that the dendritic cell compositions can be injected directly or near to the site of a tumor to induce an immunological response against antigens in the tumor (see page 6, in particular). WO 00/15264 teaches administration of the dendritic cells as a suspension with a pharmaceutically acceptable solution, in combination with other cytokines which promote the ability of the dendritic cells to activate an immune response (see page 8, in particular). WO 00/15264 teaches that IL-12 is a dendritic cell produced cytokine that enhances T cell responses (i.e. promotes the ability of dendritic cell to induce T cell responses, see page 2, in particular).

WO 00/15264 does not explicitly teach IL-12 as the cytokine to be used in combination with the dendritic cells.

Brunda et al. teach that IL-12 can be injected directly into the tumor region to treat tumors, and that IL-12 acts through T cell immune mediated mechanisms (see page 1228, in particular). The '714 patent teaches that pharmaceutical compositions of human IL-12 for therapy can comprise from about 0.1 to about 1 mg/ml of IL-12, and can be administered at a dosage of about 1mg/kg (see columns 6-7 in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to prepare the therapeutic compositions of WO 00/15264, using IL-12 as the cytokine for use in combination with the dendritic cells. The ordinary artisan would have been motivated to do so, since WO 00/15264 teaches administration in combination with cytokines which promote the activation of an immune response, and Brunda et al. and WO

00/15264 teach that IL-12 has anti-tumor activity by promoting the T cell immune responses (i.e. a dendritic cell induced immune response). Furthermore, optimizing the dose of IL-12 in the dendritic cell composition is routine, and the dosages recited (i.e. about 1mg) are well within the purview of the ordinary artisan based on the teaches of the '714 patent. Furthermore, it would have been obvious to enclose the dendritic cell suspension of WO 00/15264 in a disposable syringe for injection.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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